

CLAIMS

What is claimed is:

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1. An antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 2, wherein said antibody or antigen-binding fragment thereof inhibits binding of a ligand to the receptor.

2. An antibody or antigen-binding fragment according to Claim 1 wherein said antibody or antigen-binding fragment thereof inhibits one or more functions associated with binding of the ligand to the receptor.

3. An antibody or antigen-binding fragment thereof according to Claim 1 wherein the mammalian CC-chemokine receptor 2 is a human CC-chemokine receptor 2.

4. An antibody or antigen-binding fragment thereof according to Claim 1 wherein the ligand is a chemokine.

5. An antibody or antigen-binding fragment thereof according to Claim 4 wherein the chemokine is selected from the group consisting of MCP-1, MCP-2, MCP-3, MCP-4 and combinations thereof.

6. An antibody or antigen-binding fragment thereof according to Claim 1, wherein said antibody or fragment is a monoclonal antibody or fragment thereof.

7. An antibody or antigen-binding fragment thereof according to Claim 1, wherein said antibody or fragment is a human antibody or fragment thereof.

8. An antibody or antigen-binding fragment thereof according to Claim 1, wherein said antigen-binding fragment is selected from the group consisting of an Fv fragment, an Fab fragment, an Fab' fragment and an F(ab')₂ fragment.

9. An antibody or antigen-binding fragment thereof according to Claim 1, wherein said antibody or fragment is a humanized antibody or fragment thereof.

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10. An antibody or antigen-binding fragment thereof according to Claim 1, wherein said antibody or fragment is a recombinant antibody or fragment thereof.

11. A test kit for use in detecting the presence of a mammalian CC-chemokine receptor 2 in a biological sample comprising

10 a) at least one antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 2, wherein said antibody or antigen-binding fragment thereof inhibits binding of a ligand to the receptor; and

b) one or more ancillary reagents suitable for detecting the presence of a complex between said antibody or antigen-binding fragment thereof and said mammalian CC-chemokine receptor 2 or a portion thereof.

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12. A method of inhibiting the interaction of a cell bearing mammalian CC-chemokine receptor 2 with a ligand thereof, comprising contacting said cell with an effective amount of an antibody or antigen-binding fragment thereof which binds to mammalian CC-chemokine receptor 2 and inhibits binding of said ligand to the receptor.

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13. A method according to Claim 12 wherein the cell is selected from the group consisting of lymphocytes, monocytes, granulocytes, T cells, basophils, and cells comprising a recombinant nucleic acid encoding CCR2 or a portion thereof.

14. A method according to Claim 13 wherein the T cells are selected from the group consisting of CD8+ cells, CD25+ cells, CD4+ cells and CD45RO+ cells.

15. A method according to Claim 12 wherein the ligand is a chemokine.

16. A method according to Claim 15 wherein the chemokine is selected from the group consisting of MCP-1, MCP-2, MCP-3, MCP-4 and combinations thereof.

17. A method of inhibiting HIV infection of a cell, comprising contacting a cell with an effective amount of a composition comprising an antibody or antigen-binding fragment thereof which binds to mammalian CC-chemokine receptor 2 and inhibits HIV entry into said cell.

10 18. A method according to Claim 17 wherein the cell is selected from the group consisting of lymphocytes, monocytes, macrophages, granulocytes, T cells, and cells comprising a recombinant nucleic acid encoding CCR2 or a portion thereof.

15 19. A method according to Claim 18 wherein the T cells are selected from the group consisting of CD8+ cells, CD25+ cells, CD4+ cells and CD45RO+ cells.

20 20. A method of treating HIV in a patient comprising administering to the patient a composition comprising an effective amount of an antibody or antigen-binding fragment thereof which binds to mammalian CC-chemokine receptor 2 and inhibits HIV entry into said cell.

20 21. A method of detecting expression of mammalian CC-chemokine receptor 2 or portion thereof by a cell, comprising:

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14. a) contacting a composition comprising a cell to be tested with an antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 2, wherein said antibody or antigen-binding fragment thereof inhibits binding of a ligand to the receptor; and

15. b) detecting binding of said antibody or antigen-binding fragment thereof, wherein the binding of said antibody or antigen-binding fragment thereof indicates the presence of said receptor or portion of said receptor on said cell.

16. 22. The method of Claim 21 wherein the composition is a sample comprising human cells.

17. 23. A method of detecting a mammalian CC-chemokine receptor 2 or portion of said receptor, comprising:

18. a) contacting a sample to be tested with an antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 2, wherein said antibody or antigen-binding fragment thereof inhibits binding of a ligand to the receptor under conditions appropriate for binding of said antibody or fragment thereof thereto; and

19. b) detecting or measuring binding of said antibody or antigen-binding fragment thereof,

20. wherein the binding of said antibody or antigen-binding fragment thereof to material in said sample is indicative of the presence of a mammalian CC-chemokine receptor 2 or portion of said receptor in said sample.

21. 24. A method according to Claim 23, wherein the sample is a cellular fraction which, in normal individuals, comprises a mammalian CC-chemokine receptor 2 or portion of said receptor.

25. A method of inhibiting a function associated with binding of a chemokine to a mammalian CC-chemokine receptor 2 or a functional portion of said receptor, comprising contacting a composition comprising the receptor or portion with an effective amount of an antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 2, wherein said antibody inhibits binding of said chemokine to mammalian CC-chemokine receptor 2 and inhibits one or more functions associated with binding of the ligand to the receptor.

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26. A method according to Claim 25 wherein the chemokine is selected from the group consisting of MCP-1, MCP-2, MCP-3, MCP-4 and combinations thereof.

10 27. A method of detecting or identifying an agent which binds a mammalian CC-chemokine receptor 2 or ligand-binding variant thereof, comprising combining

a) an agent to be tested;

b) an antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 2, wherein said antibody or antigen-binding fragment thereof inhibits binding of a ligand to the receptor; and

15 c) a composition comprising a mammalian CC-chemokine receptor 2 or a ligand-binding variant thereof,

under conditions suitable for binding of said antibody or antigen-binding fragment to said mammalian CC-chemokine receptor 2 or ligand-binding variant thereof, and detecting or measuring binding of said antibody or antigen-binding fragment to said mammalian CC-chemokine receptor 2 or ligand-binding variant thereof.

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28. A method according to Claim 27 wherein the formation of a complex between said antibody or antigen-binding fragment and said mammalian CC-chemokine receptor 2 or ligand-binding variant is monitored, and wherein a decrease in the

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amount of complex formed relative to a suitable control is indicative that the agent binds said receptor or ligand-binding variant thereof.

29. A method according to Claim 27 wherein the composition comprising a mammalian CC-chemokine receptor 2 or a ligand-binding variant thereof is a cell bearing recombinant CC-chemokine receptor 2 or ligand-binding variant thereof.

5 30. A method according to Claim 29, wherein the composition comprising a mammalian CC-chemokine receptor 2 or a ligand-binding variant thereof is a membrane fraction of said cell bearing recombinant CC-chemokine receptor 2 or ligand-binding variant thereof.

10 31. A method according to Claim 27 wherein the antibody or antigen-binding fragment thereof is labeled with a label selected from the group consisting of a radioisotope, spin label, antigen label, enzyme label, fluorescent group and chemiluminescent group

15 32. A method according to Claim 27 wherein the agent is an antibody having specificity for a mammalian CC-chemokine receptor 2 or antigen-binding fragment thereof.

20 33. ✓ A method of inhibiting HIV infection in a patient, comprising administering to the patient a composition comprising an effective amount of an antibody or antigen-binding fragment thereof which binds to mammalian CC-chemokine receptor 2 and inhibits binding of HIV to the receptor.

25 34. ✓ A method of inhibiting leukocyte trafficking in a patient, comprising administering to the patient a composition comprising an effective amount of an

antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 2 and inhibits binding of a ligand to the receptor.

35. A method according to Claim 34 wherein the ligand is a chemokine.

36. A method according to Claim 35 wherein the chemokine is selected from the group consisting of MCP-1, MCP-2, MCP-3, MCP-4 and combinations of the foregoing.

5 37. A composition comprising an antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 2, wherein said antibody or antigen-binding fragment thereof inhibits binding of a ligand to the receptor, and an optional physiologically acceptable vehicle.

38. An antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 2, wherein said antibody or antigen-binding fragment thereof inhibits binding of a ligand to the receptor with an IC_{50} of less than about 1.0 $\mu\text{g}/\text{ml}$.

15 39. An antibody or antigen-binding fragment thereof according to Claim 38 wherein the IC_{50} is less than about 0.05 $\mu\text{g}/\text{ml}$.

40. An antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 2, wherein said antibody or antigen-binding fragment thereof inhibits binding of a ligand to the receptor, and wherein the antibody or antigen-binding fragment binds the receptor with an affinity of at least about 0.1
20 $\times 10^{-9} \text{ M}$.

41. An antibody or antigen-binding fragment thereof according to Claim 40, wherein the affinity is at least about 1×10^{-9} M.
42. An antibody or antigen-binding fragment thereof according to Claim 40, wherein the affinity is at least about 3×10^{-9} M.
- 5 43. A method of treating a CC-chemokine receptor 2-mediated disorder in a patient, comprising administering to the patient an effective amount of an antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 2, wherein said antibody or antigen-binding fragment thereof inhibits binding of a ligand to the receptor.

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